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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	23

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/801,115	MA ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-36,38-52 and 54-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-36,39-46,48-52 and 54-63* is/are rejected.

7)☐ Claim(s) *38 and 47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *30 November 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *22* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendments of 30 November 2003 (Paper No. 16) and 23 January 2003 (Paper No. 17) has been entered in full. Claims 34-72 are added. Claims 43, 51, 56-57, and 59 are amended. Claims 1-33, 37, 53, and 64-72 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 34-36, 38-52, and 54-63 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to the drawings at pg 5 of the previous Office Action (Paper No. 12, 30 July 2002) is withdrawn in view of the submitted corrected Figures 5A-5C and 5H-5I (Paper No. 16, 30 November 2002).

2. The objections to the specification at pg 5 of the previous Office Action (Paper No. 12,30 July 2002) are *withdrawn* in view of the amended specification and title (Paper No. 16, 30 November 2002).

3. The objection to claim 1 at pg 5 of the previous Office Action (Paper No. 12, 30 July 2002) is *withdrawn* in view of the cancelled claim (Paper No. 16, 30 November 2002).

4. The rejections of claims 1-5, 9-10, and 14-16 under 35 U.S.C., first paragraph (scope of enablement and written description) as set forth at pg 6-12 of the previous Office Action (Paper No. 12, 30 July 2002) are *withdrawn* in view of the cancelled claims (Paper No. 16, 30 November 2002). Please see section on 35 U.S.C. § 112, first paragraph, below.

5. The rejection of claims 1-5, 9-10, and 14-16 under 35 U.S.C. § 112, first paragraph (deposit rules) as set forth at pg 12-13 of the previous Office Action (Paper No. 12, 30 July 2002) is *withdrawn* in view of the cancelled claims and declaration of biological culture deposit (Paper No. 14; 30 November 2002).

6. The rejection of claims 1-4, 9-10, and 14-16 under 35 U.S.C. § 103(a) as set forth at pg 13-15 of the previous Office Action (Paper No. 12, 30 July 2002) is *withdrawn* in view of the cancelled claims (Paper No. 16, 30 November 2002). Please see section on 35 U.S.C. § 103(a), below.

Sequence Compliance

7. The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (Paper No. 16, 30 November 2002; Paper No. 20, 05 April 2003) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (Paper No. 12, 30 July 2002) are withdrawn.

Information Disclosure Statement

8. The information disclosure statement filed 30 November 2002 (Paper No. 15) fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Specifically, two references (AG and AK), were not attached to the newly submitted PTO-1449 form. Applicant is encouraged to re-submit the two references (and if received, the USPTO postcard indicating that the references were submitted).

Claim Objections

9. Claim 51 is objected to because of the following informalities:

9a. Line 2 of claim 51 should be amended to recite "SEQ ID NO: 1" rather than "sequence ID NO: 1".

9b. Claims 38 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

Appropriate correction is required.

35 USC § 112, first paragraph

10. Claims 51-52, 54-59, and 63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide fragment of the sequence as set forth in SEQ ID NO: 1 or the complement thereof that hybridizes to the sequence as set forth in SEQ ID NO: 1 under wash conditions of 125mM sodium phosphate (pH7.2), 0.05 mM EDTA, and 2.5% SDS at 65°C., wherein said fragment is at least 20 nucleotides in length, does not reasonably provide enablement for an isolated polynucleotide fragment of the sequence as set forth in sequence ID NO: 1 or its compliments capable of hybriding to (a) a polynucleotide encoding the polypeptide consisting of the amino acid sequence as set forth in SEQ ID NO: 2; or (b) a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit NO. 0392, under wash conditions of 125 mM sodium phosphate (pH7.2), 0.05 mM EDTA, and 2.5% SDS at 65°C. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to an isolated polynucleotide fragment of the sequence as set forth in sequence ID NO: 1 or its compliments capable of hybriding to (a) a polynucleotide encoding the polypeptide consisting of the amino acid sequence as set forth in SEQ ID NO: 2; or (b) a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit NO. 0392, under wash conditions of 125 mM sodium phosphate (pH7.2), 0.05 mM EDTA, and 2.5% SDS at 65°C. The claims also recite vectors containing the isolated polynucleotide and host cells.

As discussed in the previous Office Action, the specification discloses that the terms "fragment", "derivative", and "analog" when referring to the polypeptide of CKLF1 means a polypeptide which retains essentially the same biological function or activity as such polypeptides (pg 10, lines 24-29). The fragment, derivative, or analog of the polypeptide of CKLF or that encoded by the deposited DNA may be one in which one or more amino acids residues are substituted with a conserved or non-conserved amino acid residue, one in which one or more amino acid residues includes a substituent group, one in which the mature polypeptide is fused with another compound, one in which the additional amino acids are fused to the mature polypeptide, and splice variants of the mature polypeptide which are lacking certain amino acid residues (pg 10, lines 32-37; pg 11, lines 1-9). However, the specification does not teach all possible fragments of SEQ ID NO: 1 that hybridize to a polynucleotide encoding the polypeptide consisting of the amino acid sequence of SEQ ID NO: 2 or a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA in CGMCC Deposit NO. 0392. Additionally, since claims of the instant application recite polynucleotide fragments hybridizing to a polynucleotide encoding the polypeptide of SEQ ID NO: 2, the claims

encompass codon degeneracy. Briefly, there are sets of three nucleotides that make up a codon and many amino acids are specified by more than one codon (degeneracy of the code; see Alberts et al. Molecular Biology of the Cell, New York: Garland Publishing, 1994; pg 106-110, Figure 3-16, 230-234). Therefore, the skilled artisan is not able to predict what the polynucleotide-encoding sequence is from an amino acid sequence and use of a degenerate sequence as a probe does not come with a reasonable expectation of success.

Furthermore, the specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error (pg 7-9). Undue experimentation would be required by the skilled artisan to generate the infinite number of polynucleotide fragments recited in the claims and to screen the same for activity. The specification fails to teach the skilled artisan how to use the claimed polynucleotide fragments to make biologically active CKLF1 without resorting to undue experimentation to determine what the specific biological activities of the CKLF1 polypeptide and all CKLF1 variants are.

Due to the large quantity of experimentation necessary to generate the infinite number of polynucleotide fragments recited in the claims, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of what the polynucleotide-encoding sequence is from an amino acid sequence and use of a degenerate sequence as a probe, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

11. Claims 60-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, the claims are directed to a method of producing a chemokine-like factor polypeptide comprising introducing the vector of claim 55 into a host cell, and expressing from the host cell or extracellular media the polypeptide encoded by said cDNA. The claims also recite a vector, host cell, and that the polynucleotide is RNA.

The specification teaches that fragments of the full length chemokine-like factor (CKLF) gene may be used as a hybridization probe for a cDNA library to isolate the full length CKLF gene and to isolate other genes which have a high similarity to the gene or similar biological activity (pg 8, lines 19-29). The specification also discloses that the polynucleotide may have at least 20 bases, preferably 30 bases, and more preferably 50 bases which hybridize to the CKLF1 polynucleotide of the present invention and which has an identity thereto, and which may or may not retain activity (pg 9, lines 12-17). The Examiner acknowledges that polynucleotide fragments may be employed as probes for the polynucleotide of SEQ ID NO: 1. However, the specification does not teach any methods or working examples that produce a CKLF1 polypeptide by introducing a vector containing any polynucleotide fragment of SEQ ID NO: 1 into a host cell and expressing the polypeptide encoded by the cDNA from the host cell. Undue experimentation would be required of the skilled artisan to generate the infinite number of polynucleotide fragments and polypeptide derivatives recited in the claims and screen same for activity. While it is known that many amino acid substitutions are generally possible in any

given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

12. Claims 51-52 and 54-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to an isolated polynucleotide fragment of the sequence as set forth in sequence ID NO: 1 or its compliments capable of hybridizing to (a) a polynucleotide encoding the polypeptide consisting of the amino acid sequence as set forth in SEQ ID NO: 2; or (b) a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit NO. 0392, under wash conditions of 125 mM

sodium phosphate (pH7.2), 0.05 mM EDTA, and 2.5% SDS at 65°C. The claims also recite a method of producing a chemokine-like factor polypeptide comprising introducing the vector of claim 55 into a host cell, and expressing from the host cell or extracellular media the polypeptide encoded by said cDNA.

The specification discloses that the terms "fragment", "derivative", and "analog" when referring to the polypeptide of CKLF1 means a polypeptide which retains essentially the same biological function or activity as such polypeptides (pg 10, lines 24-29). The fragment, derivative, or analog of the polypeptide of CKLF or that encoded by the deposited DNA may be one in which one or more amino acids residues are substituted with a conserved or non-conserved amino acid residue, one in which one or more amino acid residues includes a substituent group, one in which the mature polypeptide is fused with another compound, one in which the additional amino acids are fused to the mature polypeptide, and splice variants of the mature polypeptide which are lacking certain amino acid residues (pg 10, lines 32-37; pg 11, lines 1-9). However, the specification does not teach functional or structural characteristics of the all claimed polynucleotide fragments in the context of a cell or organism. The description of one chemokine-like polynucleotide species (SEQ ID NO: 1) and one polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all fragments.

Simply reciting hybridization conditions in the claims does not yield adequate written description of the polynucleotides encompassed. The claims encompass an infinite number of polynucleotide fragments that hybridize to a polynucleotide encoding the polypeptide consisting of the amino acid sequence as set forth in SEQ ID NO: 2 or a polynucleotide encoding a mature

polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit NO. 0392. These polynucleotide fragments may be structurally and functionally divergent from the polynucleotide of SEQ ID NO: 1. Furthermore, the specification's general discussion of making and screening for variants (pg 7-9) constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed fragments.

Claim Rejections - 35 USC § 103

13. Claims 34-36, 39-46, 48-50, 51-52, and 54-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al. (Genbank Accession No. AA455042) and Sibson et al. (WO 94/01548). The basis for this rejection is set forth for originally examined claims 1-4, 9-10, and 14-16 at pg 13-15 of the previous Office Action (Paper No. 12, 30 July 2002).

Hillier et al. teaches a polynucleotide that encodes a mature polypeptide having the amino acid sequence of SEQ ID NO: 2 of the instant application (See sequence alignment attached to previous Office Action as Appendix B; see nucleotides 60-356 of Hillier et al. and amino acids 1-99 of SEQ ID NO: 2 of the instant application.)

Hillier et al. does not disclose expression vectors, host cells or a method of producing a polypeptide.

Sibson et al. discloses that it is generally useful to place a desired cDNA sequence into an expression vector, host cell, and express the encoded protein (see pages 8-13).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use Hillier et al.'s cDNA and the expression vector, host cell, and method

of expressing and then isolating the encoded polypeptide as taught by Sibson et al. in view of Sibson's suggestion that it would be desirable to do so, as cited above.

Applicant's arguments (Paper No. 16, 30 November 2002), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that Hillier et al. does not teach the claimed isolated polynucleotide encoding the polypeptide consisting of the amino acid sequence as set forth in SEQ ID NO: 2 nor the claimed isolated polynucleotide encoding a mature polypeptide of the amino acid sequence expressed by the cDNA contained in CGMCC Deposit NO. 0392. Applicant argues that Hillier et al. teaches away from Applicant's invention because Hillier et al. teach a full length nucleotide sequence of 427 nucleotides., which encodes a polypeptide of 152 amino acids. Applicant contends that Hillier et al. does not disclose Applicant's claimed isolated polynucleotide encoding the polypeptide consisting of the amino acid sequence as set forth in SEQ ID NO: 2 (99 amino acids) or an isolated polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit NO. 0392.

Applicant's arguments have been fully considered but are not found to be persuasive. It is noted to Applicant that, for example in claim 34(b), which recites "a polynucleotide encoding a mature polypeptide *having* the amino acid sequence..." the term "having" is interpreted by the Examiner as open terminology. Therefore, the term "having" still allows the inclusion of other, larger nucleotide sequences that encode the protein. (See MPEP § 2111.03; *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1573, 43 USPQ2d 1398, 1410 (Fed. Cir. 1997).)

Please note that this issue could be overcome by amending the claims to recite "consisting of" rather than "having".

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
July 3, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER